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Editorial

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The surgical management of high-risk neuroblastoma

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Editorial

Neuroblastoma is the most common solid, extracranial malignancy of childhood. It is a heterogeneous tumor derived from neural crest cells. While it can develop anywhere along the sympathetic ganglion chain, it most commonly develops in the retroperitoneum within the adrenal gland. Patients with low- and intermediate-risk neuroblastoma have 5-year survival rates of greater than 90%, however despite aggressive multimodal therapies, the 5-year survival rate in those with high-risk neuroblastoma remains at 40-50%. Surgical resection remains a cornerstone of therapy in the young patients suffering from this complex disease.

In the United States, the current collaborative treatment of high-risk disease typically is divided into three phases of multimodal treatment: induction, consolidation, and maintenance. The induction phase involves the use of 5-6 cycles of chemotherapy. Resection of the primary tumor and any large metastases is generally performed after the 4th-5th cycle of chemotherapy when the tumor has shrunk to its smallest size. The consolidation phase includes the use of stem cell transplantation and radiation therapy. In preparation for stem cell transplantation, the patient undergoes myeloablative therapy using melphalan which diminishes bone marrow cells and helps to eradicate residual disease. Peripheral blood stem cells harvested during the induction phase are then infused to replenish the bone marrow. Radiation therapy is directed at the primary tumor bed as well as any MIBG-positive areas of bony metastases. During the maintenance phase, the patient is treated with isotretinoin to induce differentiation of any residual disease. Recently approved by the Food and Drug Administartion (FDA) as the first drug for treating pediatric cancer, the anti-GD2 antibody ch14.18, which targets a surface disialoganglioside present on all neuroblastoma cells, has been introduced into clinical practice with good early results.

Prior to surgery, we recommend obtaining an abdominal and pelvic CT scan with oral and intravenous contrast to re-evaluate the size of the primary tumor after chemotherapy, to identify sites of tumor invasion, and to delineate the course of any associated major blood vessels. A complete blood count should be sent to verify that the patient has an absolute neutrophil count of at least 1000. Type and cross-matched blood should be made available prior to surgery. Generally, an epidural catheter is placed for intra-operative and post-operative pain management. A ureteral stent may be placed if the tumor is adjacent to or involves the ureters.

The surgical approach to high-risk abdominal tumors is determined by tumor size and stage. Prior to chemotherapy, if the tumor appears to be stage 2, a primary resection should be considered. Those tumors that are deemed unresectable are typically biopsied and the chemotherapeutic regimen is begun. The goal of surgery for most high-risk neuroblastomas is a gross total resection with removal of any local lymphatic spread. Since most intraabdominal tumors arise within the adrenal gland, an en bloc adrenalectomy is often required. Unfortunately, it is very common for the tumor to encase the major mesenteric and renal vessels making resection quite challenging.

When initiating the procedure, we enter the abdomen using a subcostal incision on the ipsilateral side extending the incision transversely through the upper epigastrium just beyond the midline. If needed, this incision is lengthened to the contralateral side for greater exposure. Alternatively, a thoracoabdominal incision can be utilized. Once the peritoneal cavity is entered, the region of the primary tumor is closely inspected. We evaluate the liver for signs of metastatic disease and biopsy any suspicious lesions. The ipsilateral colon is mobilized medially to access the retroperitoneum. The spleen, pancreas, and right lobe of the liver may also need to be mobilized as well depending on the side of the tumor. Our second objective is to remove the primary tumor while preserving the ipsilateral kidney which should be possible in most cases. In the few cases, where a dissection plane between the kidney and tumor cannot be established, a partial or complete nephrectomy should be performed as needed. Typically, the tumor can be freed from its lateral and posterior attachments without damaging any major structures. If the mass is attached to the diaphragm superiorly, the diaphragm should be resected with the tumor en bloc. Our attention is then focused medially which usually is the most challenging part of the resection as this side of the tumor can involve critical blood vessels. We first isolate the distal and proximal aspects of the involved major vessels. In tumors that encase, major vessels, we use a clamp to bluntly separate or bi-valve the tumor from the underlying blood vessel proximally to distally along the length of the vessel. When most of the tumor has been mobilized, we identify an area where the tumor can be safely transected medially. At this point, we meticulously inspect the tumor bed to identify and resect and remaining gross disease. Any small vessels or lymphatics encountered are ligated with silk ties and titanium clips to help prevent the development of bloody or chylous ascites.

Depending on the difficulty of the surgical resection, the incidence of complication and blood loss, postoperative admission to the pediatric intensive care unit may be necessary. However, most patients will be able to recover sufficiently on a surgical inpatient floor. Postoperatively, we attempt a fast-track management plan and avoid nasogastric tubes and excessive narcotic use. The patients are started

early on a clear liquid diet and ambulation is encouraged as soon as possible. If the patient is tolerating a regular diet without evidence of postoperative complication, we find that it is reasonable to allow chemotherapy treatment to resume after one week and radiation therapy after one month.

The resection of high-risk tumors can be challenging even in the most experienced of hands. It is essential that adequate exposure is obtained and a meticulous dissection including the skeletonization of major vessels is performed to avoid significant postsurgical morbidity. Continued research into the optimal medical and surgical management of high-risk neuroblastoma is vital to increase the survival rate of this aggressive disease.

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Conflicts of interest

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